

ADT US 5219740 A US 1987-14579 19870213

PRAI US 1987-14579 19870213

IC ICM C12N005-10

ICS C12N015-86

AB US 5219740 A UPAB: 19931116

A novel process (I) of gene transfer into diploid fibroblasts in vitro comprises genetically modifying diploid fibroblasts explanted from a mammalian subject by a process consisting of introducing into the fibroblasts a retroviral construct comprising a first nucleotide sequence encoding a first expression prod., a viral long terminal repeat (LTR) and a promoter sequence upstream of the first nucleic acid sequence, and a viral LTR and a polyadenylation sequence downstream of the first nucleotide sequence, where the retroviral construct lacks one or more of the gag, pol and env sequence required for retroviral replication, by contacting the fibroblasts with the retroviral construct in a virus-containing medium having a viral titer of at least 10 power 5 cfu/ml on NIH 3T3 fibroblasts to produce a population of fibroblasts at least 10% of which express the first expression prod..

USE/ADVANTAGE - The process provides for mammalian gene therapy. The explanted fibroblasts are genetically modified to introduce gene of therapeutic importance so as to permit and facilitate the expression of the introduced gene(s) following implantation of the modified fibroblasts into the patient. The recipient of the modified fibroblasts will typically be deficient in the therapeutic prod., e.g. an enzyme, hormone or precursor, e.g. adenosine deaminase, purine nucleoside phosphorylase and blood clotting factor VIII and IX.

Dwg.0/5

FS CPI

FA AB

MC CPI: B04-B04A3; C04-B04A3; B11-C09; C11-C09; D05-H12

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(FILE 'HOME' ENTERED AT 11:20:05 ON 24 MAY 2005)
 SET COST OFF

FILE 'BIOSIS' ENTERED AT 11:20:19 ON 24 MAY 2005

E SIMMONS P/AU

L1 282 S E3-E14,E16-E19

E GRONTHOS S/AU

L2 35 S E3,E4

E ZANNETTINO A/AU

L3 50 S E3-E6

E ZANETINO A/AU

E ZANNETINO A/AU

L4 3 S E3-E5

E ZANETTINO A/AU

L5 322 S L1-L4

18 S L5 AND ?MESENCHYM?

L6 26 S L5 AND CFU

L7 10 S L5 AND CFU F

L8 7 S L5 AND CFU(L) FIBROBLAST?

L9 20 S L5 AND COLON? FORM? UNIT?

L10 9 S L10 AND (F OR FIBROBLAST?)

L11 28 S L6,L8,L9,L11

L12 17 S L6-L11 NOT L12

L13 232 S L5 AND PY<=2000

L14 11 S L5 AND P/DT

SEL DN AN 1 4 8
 L16 3 S L15 AND E1-E6
 L17 10 S L14 AND L12
 L18 13 S L16,L17
 L19 18 S L12 NOT L18
 L20 99 S L14 AND 00520/CC
 L21 116 S L14 AND (CONGRESS? OR CONFERENC? OR POSTER? OR SYMPOS? OR MEE
 L22 17 S L21 NOT L20
 L23 2 S L22 AND CONFERENCE?/DT
 L24 101 S L20,L23
 L25 8 S L24 AND L6-L13,L17-L19
 L26 7 S L25 NOT LTC/TI
 L27 15 S L18,L26
 L28 14 S L27 NOT CFU S
 L29 14 S L28 AND L1-L28

FILE 'BIOSIS' ENTERED AT 11:31:32 ON 24 MAY 2005
 L30 325 S CFU F OR COLON? FORM? UNIT? F
 L31 110 S CFU FIBROBLAST? OR COLON? FORM? UNIT? FIBROBLAST?
 L32 277 S L30,L31 AND PY<=2000
 L33 414 S COLON? FORM? UNIT? (L)FIBROBLAST?
 L34 317 S L33 AND PY<=2000
 L35 408 S L33,L34 NOT L29
 L36 39 S L35 AND ?MESENCHYM?
 L37 142 S L35 AND (LFA 3 OR THY 1 OR STRO1 OR STRO2 OR STRO())(1 OR 2) O
 L38 3 S L35 AND PEROXISOM? PROLIFERAT? ACTIVAT? RECEPTOR?
 L39 8 S L35 AND (CD ANTIGEN OR CD49# OR CD29 OR CD18 OR CD61 OR 6 19
 L40 32 S L35 AND ?MARKER?
 L41 28 S L35 AND ?ANTIGEN?
 L42 166 S L37-L41
 L43 32 S L36 AND L42
 L44 7 S L36 NOT L43
 L45 198 S L35 AND STROMA?
 L46 48 S L45 AND L36,L40,L41
 L47 23 S L46 NOT L43,L44
 SEL DN AN 2 6 9 10 11 13 20 22 23
 L48 9 S L47 AND E7-E27
 SEL DN AN L43 3-5 8 9 13 30 31
 L49 24 S L43 NOT E28-E43
 L50 33 S L48,L49 AND L1-L49
 L51 7 S L50 AND ENRICH?
 L52 21 S L50 AND ?CULTUR?
 L53 21 S L51,L52
 L54 12 S L50 NOT L53
 L55 33 S L53,L54

FILE 'WPIX' ENTERED AT 11:47:30 ON 24 MAY 2005
 L56 12 S L30/BIX OR L31/BIX OR L33/BIX OR (CFU (L) FIBROBLAST?)/BIX
 L57 7 S L56 AND ?MESENCHYM?/BIX
 L58 8 S L56 AND C12N/IPC
 L59 11 S L57,L58
 L60 12 S L56-L59
 L61 1 S L60 AND (SIMMONS P? OR GRONTHOS S? OR ZANNETTINO ? OR ZANETTI
 L62 1 S L60 AND MEDVET?/PA
 L63 1 S L61,L62
 L64 11 S L60 NOT L63

FILE 'WPIX' ENTERED AT 11:54:28 ON 24 MAY 2005

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of)

IT Antigens
 RL: PROC (Process)
 (VLA-1, of bone marrow of human, cellular localization of)

IT Antigens
 RL: PROC (Process)
 (VLA-2, of bone marrow of human, cellular localization of)

IT Antigens
 RL: PROC (Process)
 (VLA-4, of bone marrow of human, cellular localization of)

IT Antigens
 RL: PROC (Process)
 (VLA-6, of bone marrow of human, cellular localization of)

IT Bone marrow, composition
 (endothelium, integrins of, of human)

IT Hematopoietic precursor cell
 (erythroid, integrins of, in humans)

IT Glycoproteins, specific or class
 RL: BIOL (Biological study)
 (integrins, $\alpha\beta$ 3, α -subunit, of
 bone marrow of human, cellular localization of)

IT Hematopoietic precursor cell
 (macrophage-monocyte-forming, integrins of, in humans)

IT Hematopoietic precursor cell
 (myeloid, integrins of, in humans)

IT Antigens
 RL: PROC (Process)
 (p150,95, of bone marrow of human, cellular localization of)

IT Bone marrow, composition
 (stroma, fibroblast colony-forming
 unit, integrins of, in humans)

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(FILE 'HOME' ENTERED AT 09:08:53 ON 24 MAY 2005)
 SET COST OFF

FILE 'HCAPLUS' ENTERED AT 09:09:05 ON 24 MAY 2005

	E SIMMONS P/AU
L1	141 S E3-E8,E12-E19
	E ZANNETTINO A/AU
L2	42 S E3-E6
	E GRONTHOS S/AU
L3	30 S E3,E4
	E ZANNET /AU
L4	2 S E6,E7
	E ZANET /AU
L5	1 S E205
	E MDEVET/PA,CS
	E MEDVET/PA,CS
L6	46 S E3-E12
L7	216 S L1-L6
L8	2 S (WO2000-AU822 OR AU99-1477)/AP,PRN
L9	2 S L7 AND L8
L10	19 S L7 AND CFU
L11	6 S L7 AND COLON? (L) FORM? (L) UNIT? (L) FIBROBLAST?
L12	6 S L10 AND F
L13	6 S L10 AND FIBROBLAST?
L14	10 S L7 AND ?MESENCHYM?

L15 16 S L11-L14
 L16 68 S L7 AND P/DT NOT L15
 L17 6 S L15 AND (PY<=2000 OR PRY<=2000 OR AY<=2000)
 L18 10 S L15 NOT L17
 L19 752 S ?MESENCHYM? (L) ?PRECURS?
 L20 710 S ?MESENCHYM? (L) ?PRECURS? (L) CELL
 L21 733 S ?MESENCHYM? (L) ?PROGENIT? (L) CELL
 L22 752 S ?MESENCHYM? (L) ?PROGENIT?
 L23 1899 S ?MESENCHYM? (L) STEM (L) CELL
 L24 510 S ?MESENCHYM? (L) (?HEMATOPOI? OR ?HAEMATOPOI? OR ?HEMAPOI? OR
 E MESENCHYM/CT
 E E8+ALL
 L25 3137 S E3+NT
 L26 977 S L25 AND L19-L24
 E STEM CELL/CT
 E E3+ALL
 L27 568 S E3,E2+NT (L) ?MESENCHYM?
 E HEMATOPOIETIC/CT
 E E21+ALL
 L28 76 S E11,E10 (L) ?MESENCHYM?
 L29 2948 S L19-L24,L26-L28
 L30 10 S L29 AND L7
 L31 2 S L30 AND L17
 L32 10 S L30 AND L15
 L33 6 S L17,L31
 L34 10 S L15,L32 NOT L33

FILE 'HCAPLUS' ENTERED AT 09:44:48 ON 24 MAY 2005

 E FIBROBLAST/CT
 E E3+ALL
 L35 9 S E4,E3 (L) COLON? FORM? UNIT
 L36 3 S E4,E3 (L) CFU
 L37 10 S L35,L36
 L38 242 S FIBROBLAST? (L) CFU
 L39 230 S FIBROBLAST? (L) COLON? FORM? UNIT
 L40 329 S L37-L39
 L41 235 S L40 AND (PY<=2000 OR PRY<=2000 OR AY<=2000)
 L42 12 S L41 AND ?MESENCHYM?
 L43 160 S L41 AND (?PRECURS? OR ?PROGENIT? OR STEM CELL)
 L44 149 S L41 AND (?HEMATOPOI? OR ?HAEMATOPOI? OR ?HEMAPOI? OR ?HAEMAPO
 L45 184 S L42-L44
 L46 20 S L45 AND (STRO1 OR STRO2 OR STRO() (1 OR 2) OR VCAM OR ICAM OR
 L47 1 S L45 AND (CD ANTIGEN OR CELL ADHESION MOLECULE OR INTERCELL? A
 L48 1 S L45 AND (PPAR? OR PPAR GAMMA 2)
 L49 33 S L46-L48,L42
 L50 30 S L49 NOT L30-L34
 L51 1 S L45 AND PEROXISOM? PROLIFERAT? ACTIVAT? RECEPTOR?
 L52 5 S L37 AND L41 NOT L30-L34
 L53 34 S L50,L51,L52
 L54 34 S L53 AND L1-L53
 L55 34 S L54 AND (CFU OR COLON? FORM? UNIT?)
 L56 25 S L55 AND (COLON? FORM? UNIT?)
 L57 9 S L55 NOT L56
 SEL DN AN 2 9
 L58 2 S L57 AND E1-E6
 L59 10 S L56 AND L42
 L60 12 S L58,L59
 L61 15 S L56 NOT L60
 SEL DN AN 1 6 11 13
 L62 4 S L61 AND E7-E18